



# NOVEL MODIFIED MSP-1 NUCLEIC ACID SEQUENCES AND METHODS FOR INCREASING mRNA LEVELS AND PROTEIN EXPRESSION IN CELL SYSTEMS

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## CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a division of U.S. Serial Number 09/175,684, filed October 20, 1998, which claims priority to U.S. Serial Number 60/085,649, filed May 15, 1998, and U.S. Serial Number 60/062,592, filed October 20, 1997, the contents of which are incorporated herein by reference.

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## BACKGROUND OF THE INVENTION

### Field of the invention

The invention relates to heterologous gene expression. More particularly, the invention relates to the expression of malaria genes in higher eukaryote cell systems.

### Summary of the related art

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Recombinant production of certain heterologous gene products is often difficult in *in vitro* cell culture systems or *in vivo* recombinant production systems. For example, many researchers have found it difficult to express proteins derived from bacteria, parasites and virus in cell culture systems different from the cell from which the protein was originally derived, and particularly in mammalian cell culture systems. One example of a

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therapeutically important protein which has been difficult to produce by mammalian cells is the malaria merozoite surface protein (MSP-1).

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Malaria is a serious health problem in tropical countries. Resistance to existing drugs is fast developing and a vaccine is urgently needed. Of the number of antigens that get expressed during the life cycle of *P. falciparum*, MSP-1 is the most extensively studied and promises to be the most successful candidate for vaccination. Individuals exposed to *P. falciparum* develop antibodies against MSP-1, and studies have shown that there is a correlation between a naturally acquired immune response to MSP-1 and reduced malaria morbidity. In a number of studies, immunization with purified native MSP-1 or recombinant fragments of the protein has induced at least partial protection from the parasite (Diggs et al, (1993) *Parasitol Today* 9:300-302) Thus MSP-1 is an important target for the

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